Docket No.: **515-4183**

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
PATENT OPERATION

In re Application of:
Maurizio Valleri &
Alessandro Tosetti

Serial No.: 09/463,586

Filed: April 24, 2000

Group Art Unit:-- 1615

Examiner:-- Pulliam,Amy

For: **PHARMACEUTICAL COMPOSITIONS CONTAINING VITAMIN D AND CALCIUM, THEIR PREPARATION AND THERAPEUTIC USE**

New York, NY 10036

Date: March 5, 2002

Commissioner for Patents
Washington, DC 20231

REQUEST FOR RECONSIDERATION

In the first paragraph on page 2 of the Office Action, Claims 1-7 were rejected under 35 U.S.C. 102(b) as being anticipated by EP 588 539A to Silver.

Reconsideration is requested.

The present invention is a pharmaceutical composition containing as active ingredients both vitamin D and a calcium salt. See claim 1 at lines 1 and 2. Silver is

limited to a disclosure of a pharmaceutical composition which comprises at least ingredients (a), (b) and (c) and, optionally the component (d) (see claim 1, page 5 and the specification page 3 line 25) which is selected from lactose, sorbitol and calcium phosphate (see claim 6, page 5). More importantly, nowhere does Silver disclose the use of calcium salt as an active ingredient. The only use of a calcium salt according to Silver is as an optional excipient or carrier.

Further, the calcium phosphate disclosed in Silver is clearly an excipient added in order to make a solid composition which specifically defined in claim 1 as "an amount sufficient to impart the characteristics of a solid to the composition". The Examiner points out that Silver teaches the use of polyethylene glycol as a stabilizer, however like the choice of calcium phosphate this is optional. Moreover, neither the use of polyethylene glycol nor the use of a 1-2 g of calcium salt to 500-1000 IU vitamin D is disclosed in any of the reported examples.

The ratio of vitamin D to calcium salt as taught by Silver only relates to its properties as an excipient, and does not teach the use of this material for its therapeutic effects as claimed in the present application. For these reasons it is requested that this ground of rejection be withdrawn.

On page 4 of the Office Action, Claims 1-8 and 13-18 were rejected under 35 U.S.C. 103(a) as being unpatentable over FR-A-2 724 844 (hereinafter FR '844).

Reconsideration is requested.

It should be noted that the FR `844 patent refers to a pharmaceutical composition which must be prepared in a "humid environment", see claim 4 page 11. However, because of the specifically chosen binders of the present invention, the application can be prepared without using water. Further, it is well known in the art that the use of humid processes of preparation can leave traces of humidity in the granulates which may result in a degradation of the vitamin D, which undergoes spontaneous oxidation.

The present invention requires the use of calcium phosphate salts and their analogues, i.e. compounds which have a high content of calcium but are insoluble. The calcium salts used in prior art normally underwent a granulation process to avoid poor flow characteristics which makes them unsuitable for processing using ordinary high output machines. However, when used in suspensions these granules increased the rate of sedimentation causing a "sand effect", thereby decreasing the uniformity of

the distribution of the active ingredients within the product. In order to make pharmaceutical compositions for oral use which do not present a "sand effect" it is necessary to identify the exact additives which show acceptable texture and at the same time allow for an industrial preparation of the composition. Therefore, it was necessary to utilize binders that would be effective in a dry environment, with high concentrations of an insoluble calcium salt such as calcium phosphates. These conditions and binders are not disclosed in FR `844.

FR `844 teaches a formulation containing not more than 500mg of elemental or calcium ion. In examples 2, 4 5 and 6 of the FR `844 patent the following quantities are reported respectively: 1.250 g of calcium carbonate (0.5 g of calcium ion); 1.5g of calcium pidolate (0.2g of calcium ion); 2 g of calcium pidolate (0.27 g of calcium ion); and 1.250 g of calcium carbonate (0.5 g of calcium ion). Further, in examples 3, 8 and 9, 3.74 g of calcium pidolate are present containing 0.5 g of calcium ion and example 7 reports 2.72 g of calcium lactate containing 0.35 g of calcium ion. This is in sharp contrast to the present Applicant's claim 1, which points out pharmaceutical compositions containing very high levels of calcium ions as compared to the vitamin D content.

As previously noted, the FR `844 patent does not disclose the use of calcium phosphate, and also requires the use of a dry and a wet binder. The procedure requires the ingredients to be dried on an air bed, unlike the procedure for making the Applicant's formulation which relies on the use of liquid binders and a homogenising step. Therefore, the claimed compositions are not made obvious by the FR `844 patent.

The present formulation overcomes the "granulation" or "sand effect" of calcium salts given in high doses necessary to provide therapeutic doses of bioavailable calcium suitable for high-speed production machines. It is maintained that the prior art references do not teach or suggest the present invention and the present claims are patentable over the references of record

In view of the foregoing, an early and favorable action is earnestly solicited.

Respectfully submitted,

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